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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/647,586	12/22/2000	Eric Argirios Kitas	RDID0063US	8561

7590

02/17/2005

Marilyn L. Amick

ROCHE DIAGNOSTICS OPERATIONS INC  
9115 Hague Road Bldg. D  
Indianapolis, IN 46250

EXAMINER

EPPS FORD, JANET L

ART UNIT

PAPER NUMBER

1635

DATE MAILED: 02/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/647,586

Applicant(s)

KITAS ET AL.

Examiner

Janet L. Epps-Ford, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 22 December 2000.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-7 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-7 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 10-02-2000.
- 4) ☒ Interview Summary (PTO-413)  
Paper No(s)/Mail Date 2-16-05
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

### DETAILED ACTION

1. The Petition under 37 CFR 1.137(b) filed February 9, 2004, to revive the instant application was granted on August 25, 2004.

#### *Sequence Listing*

2. A sequence listing in paper and computer readable form submitted by Applicants on 7-23-04 was entered 7-29-04.

#### *Specification*

3. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

#### *Claim Rejections - 35 USC § 112*

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 6-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 6 recites wherein R<sup>3</sup> is Gln-Gln-Arg-Lys-Arg-Lys-Ile-Trp-Ser-Ile-Leu-Ala-Pro-Leu-Gly-Thr-Thr-Leu-Val-Lys-Leu-Val-Ala-Gly-Ile-NH-CH[CONH<sub>2</sub>]-CH<sub>2</sub>-. Claim 7 recites wherein R<sup>3</sup> is D-Gln-D-Gln-D-Arg-D-Lys-D-Arg-D-Lys-D-Ile-D-Trp-D-Ser-D-Ile-D-Leu-D-Ala-D-Pro-D-Leu-D-Gly-D-Thr-D-Thr-D-Leu-D-Val-D-Lys-D-Leu-D-Val-D-Ala-D-Gly-D-Ile-NH-CH[CONH<sub>2</sub>]-CH<sub>2</sub>-. It is noted that there appears to be a bond located at the end of the structures set forth in claims 6 and 7, however it is unclear if this bond is intended to incorporate another molecule, or if this bond is the same bond set forth in formula I between the X and R<sup>3</sup>

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moieties (i.e. X—R<sup>3</sup>). Additionally, if the compositions of the instant invention are intended to have a structure like that set forth in formula IV of the specification as filed (see page 7), then it appears that the structure set forth in claim 7 for the R<sup>3</sup> moiety is incorrect since it comprises an additional CH group located in the structure: D-Gln-D-Gln-D-Arg-D-Lys-D-Arg-D-Lys-D-Ile-D-Trp-D-Ser-D-Ile-D-Leu-D-Ala-D-Pro-D-Leu-D-Gly-D-Thr-D-Thr-D-Leu-D-Val-D-Lys-D-Leu-D-Val-D-Ala-D-Gly-D-Ile-NH-CH[CONH<sub>2</sub>]-CH-(CH<sub>2</sub>)<sub>2</sub>-.

### *Claim Rejections - 35 USC § 103*

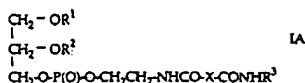
6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Legendre et al. in view of Juvvadi et al. and Densmore et al. (US Patent No. 6,106,859).

The instant claims are drawn to compositions comprising a peptide lipid conjugate according to formula I as recited in claim 1 and a protein hydrolysate. Although, the peptide structures set forth in claims 6-7 are unclear as stated in the above rejection under 35 USC 112, 2<sup>nd</sup> paragraph, to the extent that structures set forth in claims 6-7 read on melittin or retromelittin the prior art is applied.

Legendre et al. disclose the production of dioleoylmelittin and its ability to form complexes with DNA. The complexes mediate efficient transfection of various cell types (see page 3, formulas IA-IIA).



wherein X is C<sub>2-10</sub> alkylene, R<sup>1</sup> and R<sup>2</sup> independently are an acyl moiety of a C<sub>12-20</sub> aliphatic carboxylic acid and R<sup>3</sup> is as defined above.

The term "C<sub>12-20</sub>" denotes a number of carbon atoms of from 12 to 20. The acyl moieties R<sup>1</sup> and R<sup>2</sup> can be a straight-chain or branched-chain, saturated or unsaturated moiety. Examples of such moieties are lauroyl, palmitoyl, stearoyl and oleoyl. In a preferred aspect, R<sup>1</sup> and R<sup>2</sup> are oleoyl. X is preferably ethylene, propylene or decamethylene. In another and preferred aspect, the invention relates to novel compounds of the formula

However, Legendre et al. does not disclose the usage of the retromelittin comprising a reversed amide backbone as recited in the instant claims. Additionally, Legendre et al. does not disclose compositions comprising a protein hydrolysate.

Juvvadi et al. describe the preparation of retro melittin and with the finding that said retromelittin retains its antibacterial activity while the toxic effect against eukaryotic cells, normally associated with melittin, is abolished (see page 8997, last paragraph). Juvvadi et al. show that preparing the retrotype of melittin can separate the two distinct functions, inherent to melittin.

Densmore et al. describe the addition of tryptone, (i.e. a protein hydrolysate) an enzymatic (tryptic) digest of casein (see col. 5, lines 38-40), to a liposomal composition. Tryptone is described as containing glutamic acid as a major amino acid component (see col. 6, lines 23-27). The addition of tryptone to the liposomal-DNA formulation resulted in 105%, 100%, and 93% retention of transfection activity, in comparison to 51%, 13%, and 6% retention of transfection activity for liposomal-DNA compositions without added tryptone (see col. 5, lines 30-49 and Figure 1).

It would have been obvious to one of ordinary skill in the art, at the time the invention was made, to modify the teachings of Legendre et al. with the teachings of Juvvadi et al. and Densmore et al. in the design of the compositions of the instant invention. One of ordinary skill in the art would have been motivated to modify the dioleoylmelittin peptide conjugated liposomal compounds disclosed by Legendre et al. with the retromelittin peptides of Juvvadi et al. because the retromelittin compounds is described to promote electrical conductivity in lipid bilayers, to possess high antimicrobial activity while having lost its hemolytic activity. The properties described of retromelittin are exactly those required for the production of a compound useful for efficient gene delivery. Furthermore, one of ordinary skill in the art would have been motivated to add a protein hydrolysate such as tryptone to the liposomal-peptide formulations of the present invention since these formulations are designed to function as carriers for transfecting a cell with a polynucleotide or other anionic macromolecule (see page 8 of the specification as filed), and the addition of tryptone is known to enhance the transfection efficiency of DNA-liposomal complexes.

Therefore, the invention as a whole would have been *prima facie* obvious over Legendre et al. in view of Juvvadi et al. and Densmore et al.

### ***Double Patenting***

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground

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provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims 1-7 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of copending Application No. 09/712,526.

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim not is patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other because claim(s) 1-7 are generic to all that is recited in claim(s) 1 of U.S. Patent Application No. 09/712,526. That is, claim(s) 1 of U.S. Patent Application No. 09/712,526 falls entirely within the scope of instant claim(s) 1-7 or, in other words, instant claim(s) 1-7 are anticipated by co-pending claim 1 of U.S. Patent Application No. 09/712,526. Specifically, the claims of the instant application are drawn to a broad genus of liposomal compounds comprising a membrane disturbing peptide as set forth by formula I in claim 1, and a protein hydrolysate. The liposomal composition set forth in claim 1 of copending application 09/712,526 is a species of the broad genus of compounds encompassed by claims 1-7 of the instant application.

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This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

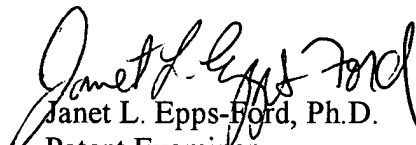
10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford, Ph.D. whose telephone number is 571-272-0757. The examiner can normally be reached on Monday-Saturday, Flex Schedule.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on 571-272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

  
Janet L. Epps-Ford, Ph.D.  
Patent Examiner  
Art Unit 1635

JLE